ALEXITHYMIA IN PATIENTS WITH HEPATITIS C: RELATIONSHIP TO DEPRESSIVE LIKE SYMPTOMS

Neil K. Rustgi, Cassie Yu, Michael J. Sheridan, Thomas N. Wise

Abstract

Objective: Hepatitis C (HCV) is often associated with symptoms of depressed mood, fatigue, sleep difficulties, impaired concentration and diminished quality of life. This study investigates the association of alexithymia with such symptoms and the burden of illness in HCV.

Method: Subjects were patients treated for HCV in a private outpatient gastroenterology practice. Those with HIV/AIDS were excluded. 83 patients completed the Brief Symptom Inventory-18 (BSI); a visual analogue scale for magnitude of depressed mood; the Toronto Alexithymia Scale-20 scale (TAS); and the Illness Effects Questionnaire (IEQ) Viral load was assessed by HCV-RNA levels.

Results: The group endorsed a generally mild to minimal distress levels due to HCV. 27% were considered clinically depressed. Alexithymic subjects had greater viral loads and endorsed significantly greater IEQ levels even when depression was controlled. Alexithymic patients reported greater depressed mood, more fatigue, and more sleep difficulties than those not alexithymic. Via logistic regression, alexithymic traits significantly predicted subjects whose depression level via BSI was one standard deviation above community norms.

Conclusions: Alexithymic traits may augment the cluster of symptoms often considered within the depressive like syndrome found in HCV patients.

Key Words: alexithymia, hepatitis c, depression, affective symptoms, fatigue

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Neil K. Rustgi, Cassie Yu, B.A., Michael J. Sheridan, Sc.D. Thomas N. Wise, M.D.[1.]

All the authors are affiliated with the Department of Psychiatry at the Inova Fairfax Hospital and the Department of Psychiatry, Virginia Commonwealth School of Medicine, School of Medicine

Corresponding author
Thomas N. Wise, M.D.
Professor of Psychiatry
Department of Psychiatry , Virginia Commonwealth University School of Medicine
3300 Gallows Road, Falls Church,Virginia 22042-3300
U.S.A.
E mail: thomas.wise@inova.org

Introduction

Hepatitis C (HCV) is a common bloodborne liver infection estimated to infect over three million individuals in the United States. (Armstrong et al. 2006a) Symptoms of fatigue, sleep difficulties, problems concentrating, and depressed mood are commonly reported by chronic HCV patients. (Armstrong et al. 2006b) Thus it is not surprising that depression and impaired quality of life are frequently cited by such patients. (Kramer et al. 2005) Factors such as interferon treatment, comorbid substance abuse and HIV/AIDS may contribute to these symptoms (Ferenci & Staufer 2008). Personality traits have received little attention as a contributing factor for these complaints. Alexithymia is a personality construct linked to amplifying somatic complaints as well as depressed mood (Mattila et al. 2008a) (Mattila et al. 2008b). This report investigates alexithymia in a cohort of HCV outpatients in a private practice setting.

Methods

A convenience sample was drawn from 100 consecutive patients with HCV at a private gastroenterology practice. Participation was voluntary. Inclusion criterion was the diagnosis of hepatitis C. Patients with HIV/AIDS were not included. 17 patients did not participate in the study. There were no demographic differences between those declining and those completing the study. The IRB of Inova Fairfax Hospital was consulted in

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the design and ethics of the study.

Demographic variables included age, gender and education. Interferon use currently or in the past was noted as was current or past psychotropic drug use. Depression if noted at all in the chart was recorded as was current or past substance abuse. Clinical liver status was measured via standard quantitative assay of HCV RNA levels utilizing polymerase chain reaction amplification (Chevaliez & Pawlotsky 2009).

Depression was measured as a clinical category as well as a dimension of dysphoric mood via two measures. For categorical designation, The Brief Symptom Inventory (BSI), an 18-question self-report inventory, measuring distress in both medical and community settings, was administered. (Derogatis 1993) The inventory assesses three separate dimensions: depression, anxiety and somatization. Adult community norms are based upon 1,325 respondents. One standard deviation above the 50th percentile of community norms is considered a clinical disorder of each domain. Although various versions of the BSI have studied oncology,substance abuse, and cardiology populations the only valid norms available are for the community norms and a psychiatric outpatient population (Clark et al. 2010, Oranta et al. 2009, Wang et al. 2010).

For dimensional assessment of depressed mood, a 100mm visual analogue scale (VAS) was utilized to assess dysphoric affect . This approach has been demonstrated to provide a valid and reliable assessment of global depressed mood (Luria 1975).

Alexithymia: Toronto Alexithymia Scale-20 The Toronto Alexithymia Scale 20(TAS-20) is a twenty-item inventory that measures alexithymia, a personality dimension that denotes difficulties in distinguishing between different emotions with insufficient recognition of physical sensations may be manifestations of such emotions. (Bagby et al. 1994a, Bagby et al. 1994b) Alexithymia also denotes difficulties in verbally expressing emotions and a cognitive style of limited fantasy and externally oriented operational thinking. Alexithymia may be considered a dimensional trait as well as a categorical designation for those that score above 61 (Mattila et al. 2009). Three subfactors have been reported for this measure but have questionable validity so that only the total TAS-20 score was utilized (Kooiman et al. 2002).

The burden of hepatitis was measured utilizing the Illness Effects Questionnaire_(IEQ). (Greenberg & Peterson 1997) The IEQ is a 40 question self report that assesses the individual's subjective appraisal of their illness in biologic, emotional and interpersonal domains. It conceptually measures the burden of a medical illness, including physical distress, fear of death and overall distress. It also measures the respondent's assessment of sleep problems attributed to the disease.

Fatigue was measured utilizing three visual analog scales that assess the impact of fatigue on the subject's relationships; their daily and their occupational activities. It has been validated for other disease states (Kos et al. 2006).

All analyses were performed using SPSS,version 14. Both parametric and nonparametric analyses were employed. When a variable appeared not to be distributed in normal manner, non parametric statistics were utilized. To examine the univariant association between variables in the study population, chi square was used for frequency data . To compare mean differences on such variables between those subjects designated as alexithymic or not alexithymic ,the Kolmogorov-Sminov test and Z statistic was used. To control for the influence of variables in predicting depression > 1 standard deviation above community norms, the independent contribution of alexithymia was examined using binary logistic regression. Statistical significant was indicated by P> 0.05.

Results (see **Table 1**)

Age, education, fatigue levels, IEQ and VAS depression levels did not differ between males and females, thus the study group was not partitioned by gender. The cohort averaged 53 years of age (S.D. 6.78) and averaged 15 years of education (S.D. 2.7). 19.5 percent of the cohort was currently on interferon, while 60 percent had been treated with such medications in the past. 36 patients (44percent) had no detectable virus. When levels of depression, IEQ burden, fatigue, somatic concern via the BSI and alexithymic traits there was no difference between those with detectable levels of virus and those with detectable viremia on measures of depression; fatigue; IEQ; and BSI somatic concern. Those with detectable viral levels were significantly more alexithymic. (P<.042, Z= -2032)

Depression, either current or past, was noted in 14 percent of the group. Substance abuse was noted in the chart in 34 percent of the group. The Illness Effects Questionnaire revealed a mean score of 30.37 (S.D. 27.3). Descriptively, this translated into 37 percent having minimal distress, 39 percent with mild distress, 18 percent with average distress and 6 percent with moderate distress. None of the subjects endorsed extreme distress due to the burden of their illness (Such categorization is discussed in the IEQ manual).

When depression was assessed categorically (those with BSI depression scores one S.D. above community norms were designated as clinically depression): 27 percent could be designated as having a depressive disorder of clinical significance, whereas 13 percent were in the borderline area of depressive categorization and 60 percent were not depressed utilizing community norms. When asked how much fatigue influenced their daily life both at home and work, as well as in social relationships, on a 100 millimeters visual analog scale, the group's average was 46.4 (SD 34.9). 26 percent noted that sleep problems were attributed this to their illness.

Utilizing alexithymia as a categorical designation, 22 percent were alexithymic, while 78 percent were not. When alexithymia was analyzed dimensionally, there was a significant relationship between IEQ score and alexithymia, even when the level of depression was controlled via partial correlational coefficient (r=.396, P<.0001). There was no significant association between drug use and categorical alexithymia (X^2 = .037,P< .847) Furthermore there was no significant different between alexithymic scores dimensionally between those with a substance abuse history and those without such a disorder.(Z=1.243.,P<.214)

When controlling for level of depression,

Table 1. *Demographic and Psychometric Variables*

Variable and Gender	Mean	Standard Deviation
Age		
Males	51.2	6.7
Females	54.7	6.8
Education (years of school)		
Males	14.6	2.6
Females	15.2	3.2
Illness Effects Questionnaire (total score)	35.92	26.9
BSI (Somatization subscale)	4.74	4.66
BSI (Depression subscale)	3.46	4.16
BSI (Anxiety subscale)	3.20	3.67
TAS (total score)	48.01	12.82
Fatigue in general	46.4	34.864
Fatigue in occupation	39.64	33.245
Fatigue in daily activities	22.46	29.86

alexithymic traits were significantly correlated with fatigue (r=.534 ,p<.0001);sleep difficulties attributed to hepatitis (r=.242,p<.05) and IEQ (burden of illness) (r=.406,p<.0001) .

Subjects designated categorically as alexithymic endorsed significantly greater fatigue; elevated levels of depression; and a greater burden of disease as measured by the IEQ. (See table with U characteristics) Sleep difficulties due to Hepatitis were significantly associated with the alexithymia designation, as well. (X^2 = 18.05, P<.0001). Sleep difficulties, were also associated with the frequency of depressive disorders (BSI categorization)

($X^{2=}$18.05, P<.0001) Finally,sleep problems were also significantly associated with alexithymic status (($X^{2=}$22.04, P<.0001).

When a logistic regression was utilized to predict the effects of personality; burden of disease (IEQ) and fatigue to ascertain whether an individual would be clinically depressed, only alexithymia emerged as a significant predictor in the model which accounted for 43 percent of the total variance. (O.R.= 1.1,P<.01).

Discussion

Hepatitis, both the disease, itself, and its treatments have been closely linked to symptoms that resemble a mood disorder such as. fatigue, sleep difficulties, generalized malaise and, as noted, depressed mood. (Fuller et al. 2009, Raison et al. 2005) The etiology of such symptoms is controversial with some suggesting it is a functional reaction to the disease and treatment ,while others recently have found mono-aminergic transporter binding alterations in the brain as a function of the viral disease (Forton 2006, Forton et al. 2006) (Weissenborn et al. 2004). The rates of depression reported vary widely from 25 to 50 percent depending upon the population studied, the criteria for depression and setting of the study. Interferon alpha therapy adds to the rates of depression as a side effect of the drug range from 16-36 percent (Angelino & Treisman 2005). Significant methodological issues have been cited as reasons for the wide variation in rates of affective disorder in such patients (Schafer et al. 2007). Besides populations with significant comorbid medical disorders such as HIV/AIDS or liver disease from substance abuse, the definition of depressive illness varies depending upon the method utilized. Furthermore, most reports have been from tertiary care centers which attract individuals with serious liver disease or from institutions such as Veterans Administration Hospitals that often have populations with high rates of comorbidity such as substance abuse and HIV/AIDS. This current report is the first in the literature from a suburban private practice of non-HIV/AIDS patients whose disease is well controlled. The rate of symptoms consistent with clinically significant depression was found to be 27 percent is at the lower end of reported rates which are usually from tertiary care centers. That most of the subjects were well controlled with limited evidence of viremia may be a factor in explaining the low rate of depression.

It is well known that certain personality characteristics may be a vulnerability factor for depressive illness. Thus, it is surprising that such personality traits have not been better studied in Hepatitis patients. Otsubo et al. reported that higher neuroticism, measured by the Eysenck Personality Questionnaire, was significantly related to an increased depressed mood and greater sleep disturbances prior to interferon therapy (Otsubo et al. 1997). In this study, those with such elevated neuroticism had scores with greater depressive ratings during the actual interferon therapy. Malyszczak et al also found neuroticism, as measured by Eysenck's Personality Questionnaire was significantly related to depression ratings. but during interferon treatment the increase in depression was independent of neuroticism levels pre-treatment (Malyszczak et al. 2006). More recently, Castellvi et al found that certain domains of the Temperament and Character Inventory – Revised were associated with both a history of previous depression

and predicted interferon-induced depression during treatment for Hepatitis C (Castellvi et al. 2009). This domain of low self-directedness has been reported to be similar to traits as measured by neuroticism (Ramanaiah et al. 2002).

Alexithymia is a personality variable that has been linked to depressed mood. (Parker et al. 2003) It also shares characteristics with both neuroticism and introversion which are two domains also linked to depression (Wise et al. 1992). Alexithymia, itself, denotes difficulty in identifying and describing feelings and difficulty in distinguishing between feelings of emotional dysphoria and somatic discomfort (Bagby et al. 1994a, Bagby et al. 1994b). It also has been suggested to be associated with complaints of poor sleep and fatigue. Furthermore alexithymia is a dimension associated with amplifying somatic complaints in both normative and clinical populations. Although some suggest alexithymia is a proxy for depression, our data reaffirm prior findings that alexithymia is a distinct construct from depression. Even when symptoms of fatigue, sleep and illness burden were controlled for depressed mood, a significant correlation with alexithymia was found. In contradistinction to the study by DeGennaro et al. sleep remained significantly correlated with alexithymia scores when the magnitude of depressed mood was controlled (DeGennaro et al. 2004) Their study was carried out in a non-clinical sample of university students. The current study is the first to assess the role of alexithymia in symptoms common in Hepatitis patients. The subset of patients with detectable viral loads were more alexithymic which could suggest that alexithymic traits are related to a secondary alexithymic process described by Freyberger as a "reaction" to the illness (Freyberger 1977, Wise et al. 1990). That alexithymic patients endorsed more depression, fatigue and burden of illness via IEQ supports this. Alexithymia has been associated with amplification of somatic symptoms (Duddu et al. 2006, Wise & Mann 1994). It may also be that be that patients alexithymic traits augment symptoms of fatigue, sleep difficulties and illness burden that are commonly seen within depressed hepatitis patients and this also contributes to elevated levels of depression. Clinically patients with significant alexithymic traits do complain of distress but are limited in explaining "why". Psychosocial or other stressors are not linked to their attributions. Thus the clinician treating such patients may have to directly ask about factors other than the physical symptoms of hepatitis to better understand the total context in which the patients present their complaints. The study is unique in that this patient population may be generalized to a broader number of patients seen in routine clinical practice with Hepatitis C. The absence of comorbid HIV/AIDS and relatively low rates of substance abuse further allow this data to be generalizable. Limitations within the study are the cross-sectional nature of the data. No control group was utilized and the BSI norms were from a healthy community sample. Future studies should investigate the longitudinal course of subjective complaints found in hepatitis and its treatments and how personality traits such as alexithymia modifies such symptoms over time.

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